

Attorney Docket No. 5218.87

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Phibbs et al.

Serial No.: 09/747,514

Filed: December 21, 2000

For: CATABOLITE REPRESSION CONTROL (crc) GENE AND PSEUDOMONAS VIRULENCE

Confirmation No. 1007

Group Art Unit: 1635

Examiner: Terra C. Gibbs

Declaration of Paul V. Phibbs, Jr., Ph.D., David N. Collier, M.D., Ph.D. and Paul W. Hager, Ph.D. Under 37 C.F.R. § 1.131

Sir:

We, Paul V. Phibbs, Jr., Ph.D., David N. Collier, M.D., Ph.D. and Paul W. Hager, Ph.D. hereby declare as follows:

1. We are the named inventors on U.S. Patent Application Serial No. 09/747,514 entitled, "Catabolite Repression Control (crc) Gene and Pseudomonas Virulence" (hereinafter, "the '514 application"), filed December 21, 2000. The subject matter of the '514 application was invented by Paul V. Phibbs, Jr., David N. Collier and Paul W. Hager. Thus, each of us is named as an inventor on the '514 application.

2. O'Toole et al. The Global Carbon Metabolism Regulator Crc Is a Component of a Signal Transduction Pathway Required for Biofilm Development by *Pseudomonas aeruginosa*. *J. Bacteriol.* 182(2): 425-431 (Jan. 2000) was co-authored by two of the inventors of the '514 application, Paul V. Phibbs, Jr. and Paul W. Hager, and three additional authors: George A. O'Toole, Karine A. Gibbs, and Roberto Kolter. At the time this article was submitted for publication, Paul V. Phibbs, Jr. was a Professor and Chairman of the Department of Microbiology and Immunology at the Brody School of Medicine at East Carolina, Paul Hager was a research instructor at the Brody School of Medicine at East Carolina University, George O'Toole was a post-doctoral candidate at Harvard Medical School and had accepted a faculty

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position at Dartmouth Medical School, Karine Gibbs was an undergraduate student, and Roberto Kolter was a faculty member at Harvard Medical School.

3. Some of the experiments described in the O'Toole et al. reference were under the direction, supervision, or the contribution of one or more of the inventors of the '514 application.

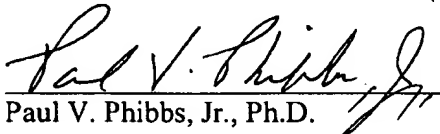
In particular, experiments leading to the discovery of methods of screening for compounds that inhibit the virulence of *Pseudomonas* bacteria comprising providing a culture medium comprising *Pseudomonas* bacteria and an amidase operon repressor, wherein the culture medium contains fluoroacetamide in an amount toxic to the bacteria in the absence of the amidase operon repressor, administering a test compound to the bacteria, and then detecting the poisoning of the bacteria by the fluoroacetamide, wherein the poisoning of the bacteria by the fluoroacetamide indicates that the test compound has antivirulence activity against *Pseudomonas* bacteria were entirely the contribution of Paul V. Phibbs, Jr. and Paul Hager. Results of some of these experiments are presented in Figure 4 of O'Toole et al.

Figure 4 shows the growth of the wild type, the *crc-24* mutant, and the *crc-24* mutant carrying pSMC31 (*crc*⁺) on minimal medium containing succinate with or without fluoroacetate (FAA). All of the strains grew equally well on minimal medium containing succinate without FAA. In contrast, the *crc-24* mutant showed no growth on the FAA-containing medium. The wild type and the *crc-24* mutant carrying the wild-type copy of *crc* on a plasmid grew well on this medium. Therefore, although the strain carrying the *crc-24* mutation was isolated in a screen for mutants unable to form a biofilm, this strain is also defective in the *Crc*-mediated, succinate-dependent catabolite repression of enzymes required for carbohydrate catabolism. These results, contributed by Paul V. Phibbs, Jr. and Paul Hager, provide a basis for methods of screening for compounds that inhibit the virulence of *Pseudomonas* bacteria.

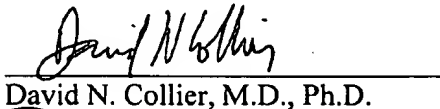
4. The authors named on the O'Toole et al. reference who are not included as inventors on the '514 application, George A. O'Toole, Karine A. Gibbs, and Roberto Kolter, did not contribute to the conception of the claimed invention set forth in the '514 application.

5. For the reasons set forth above, the inventors named on the '514 application are the true inventors thereof, and two of the three inventors are also co-authors of the O'Toole et al. reference cited in the rejections under 35 U.S.C. §103(a) and 35 U.S.C. § 102(a).

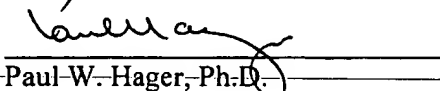
6. We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.


Paul V. Phibbs, Jr., Ph.D.

12/10/03
Date


David N. Collier, M.D., Ph.D.

Dec 10 2003
Date


Paul W. Hager, Ph.D.

Dec. 10, 2003
Date